

REMARKS

The Office Action dated December 19, 2001 has been received and reviewed. Claims 1-19 and 22-24 are pending in the present application. Claims 20 and 21 have been previously cancelled. All claims stand rejected. The application is to be amended as previously set forth. All amendments and claim cancellations are made without prejudice or disclaimer. As required by 37 C.F.R. § 1.121, a version of the amended claims with markings to clearly show the changes made is attached hereto as Appendix C. Reconsideration is respectfully requested in view of the amendments and remarks herein.

The draftsman has objected to the drawings due to an unacceptable left margin on FIG. 4. Formal drawings are submitted herewith that are believed to correct this inadvertent error. Accordingly, the objection is believed to be overcome.

Claims 1-12 and 22 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Xiang et al. (1994; *Journal of Biological Chemistry*, Vol. 269, No. 22, pp. 15,786-15,794) ("Xiang"). Further, claims 13-16, 23 and 24 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Xiang. Applicants respectfully traverse the rejections as set forth herein.

Xiang discloses that multiple mRNAs may be transcribed from multiple duplicated genes and that, due to alternative splicing events, these transcripts may be translated into PITSLRE protein kinase isoforms ranging in size from 50 to 110 kDa. Most of the resulting isoforms contain the p58^{GTA} open reading frame (ORF) and p58^{GTA} activity appears to be involved.

In contrast, as amended herein, claim 1 recites an isolated and/or recombinant nucleotide sequence enabling a G2/M cell cycle dependent initiation of translation of mRNA, wherein the isolated or recombinant nucleotide sequence is an internal ribosomal entry site (IRES) sequence which initiates mRNA translation in a eukaryotic cell. Xiang is devoid of any teaching or suggestion of initiating mRNA translation in a eukaryotic cell. Further, Xiang contains no teaching or suggestion regarding IRES sequences that initiate mRNA translation in eukaryotic cells as recited in amended claim 1. Additionally, such would not have been obvious in view of Xiang since Xiang does not concern IRES sequences or mRNA translation at all.

As amended herein, claim 4 recites an isolated and/or recombinant nucleic acid molecule encoding at least a functional part of an eukaryotic IRES, the site (in a mitotic PITSLRE protein kinase gene) comprising SEQ ID NO:1 or a functional part of SEQ ID NO:1, wherein the eukaryotic ribosomal entry site initiates mRNA translation in a eukaryotic cell. Xiang contains no teaching or suggestion regarding internal ribosomal entry sites that initiate mRNA translation in eukaryotic cells as recited in amended claim 4. Further, such would not have been obvious in view of Xiang as Xiang is not concerned with internal ribosomal entry sites or mRNA translation in eukaryotic cells. Claims 5, 6 and 7 depend from claim 4 and, thus, Xiang does not anticipate nor render obvious these claims for at least the reasons stated with regard to claim 4.

Claims 11, 12 and 14 recite a chimeric gene, a vector and a eukaryotic host cell, respectively, including (at least) the nucleotide sequence of claim 1. Xiang does not teach or suggest the use of chimeric genes, vectors or eukaryotic host cells containing, in part, nucleotide sequences which initiate mRNA translation in eukaryotic cells. Xiang is void of any teaching or suggestion regarding eukaryotic mRNA translation or translation initiation in eukaryotic cells. Further, Xiang lacks any teaching or suggestion regarding chimeric genes and/or eukaryotic host cells which contain sequences that initiate mRNA translation in eukaryotic cells. While Xiang does contain some disclosure of a vector containing a particular PITSLRE isoform, the particular isoform has no indicated mRNA translation functionality. Claims 23 and 24 depend from claim 11 and claim 15 depends from claim 14. Accordingly, Xiang does not anticipate nor render these claims obvious for at least the reasons stated with respect to claims 11 and 14.

Claim 13 recites a vector comprising the nucleotide sequence of claim 1 and a promoter. Not only does Xiang contain no teaching or suggestion regarding nucleotide sequences which initiate mRNA translation in eukaryotic cells, the reference contains no teaching regarding a promoter coupled to such sequences.

Claim 16 of the present application recites a method for cap-independent translation of mRNA in a cell, comprising introducing into the cell an expression vector comprising a translation control element which comprises a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:4, and both SEQ ID NO:1 and SEQ ID NO:4. Xiang lacks any teaching or

suggestion concerning methods of mRNA translation or translation initiation in eukaryotic cells. Thus, it is respectfully submitted that claim 16 is neither anticipated by, nor obvious in view of, Xiang.

For at least these reasons, the rejections of claims 1, 4-7 and 11-16 are believed to be overcome, and the claims are believed to be in condition for allowance. Such favorable action is respectfully requested. Claims 2, 3, 8-10 and 22 have been canceled by way of this amendment and, thus, the rejections of these claims have been rendered moot.

Claims 17-19 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Xiang in view of Parsels et al. (1998; *Cancer Journal from Scientific American*, Vol. 4, No. 5, pp. 287-295) (“Parsels”). Applicants respectfully traverse this rejection for the below-stated reasons.

Claim 17 recites a method of inducing a cell cycle dependent initiation of translation in a eukaryotic cell, the method comprising introducing the isolated and/or recombinant nucleotide sequence of claim 1 into the eukaryotic cell. Xiang, even in combination with Parsels, lacks any teaching or suggestion concerning methods of cell cycle dependent initiation of translation in eukaryotic cells which comprise introducing the nucleotide sequence of claim 1 into the cell. Neither reference recognizes that a nucleotide sequence as recited in claim 1 is capable of initiating cell cycle dependent translation of mRNA in eukaryotic cells. Accordingly, it is believed that claim 17 is not obvious in view of these references. This claim is believed to be in condition for allowance and such favorable action is respectfully requested. Claims 18 and 19 have been canceled by way of this amendment and, thus, the rejection of these claims has been rendered moot.

By way of this amendment, claims 25-36 have been added to the present application. Claim 25 recites an isolated and/or recombinant nucleic acid molecule selected from the group consisting essentially of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, or combinations thereof, the nucleic acid molecule initiating the translation of mRNA in a eukaryotic cell. Claim 26 recites a method of inducing a cell cycle dependent initiation of translation in a eukaryotic cell comprising introducing the isolated and/or recombinant nucleic acid molecule of claim 25 into the eukaryotic cell. Claims 27 recites a chimeric gene comprising at least the nucleic acid molecule of claim 25, claims 28 and 29 recite a vector comprising at least the nucleic acid molecule of claim 25, claim 30 recites a

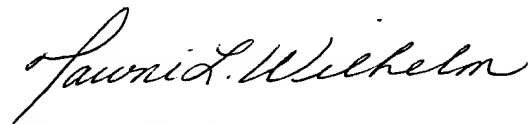
eukaryotic host cell comprising the nucleic acid molecule of claim 25 and claim 31 recites an expression system comprising the eukaryotic host cell of claim 30. Claims 32 and 33 recite a vector comprising at least the chimeric gene of claim 27, claim 34 recites a eukaryotic host cell comprising the chimeric gene of claim 27 and claim 35 recites an expression system comprising the eukaryotic host cell of claim 34. Claim 36 recites an expression system comprising the eukaryotic host cell of claim 24.

It is respectfully submitted that each of newly added claims 25-36 contain no new matter and are supported by the specification as filed.

CONCLUSION

In view of the amendments and remarks, the claims are believed to be in condition for allowance and an early notice thereof is respectfully solicited. Should the Examiner determine that additional issues remain which might be resolved by a telephone conference, the Examiner is invited to contact applicants' attorney at the address or telephone number given herein.

Respectfully submitted,



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Date: June 19, 2002

Enclosures: Petition for Three-Month Extension of Time
Check No. 2552 in the amount of \$460.00
Transmittal of Formal Drawings Prior to Notice of Allowance
Substitute Sequence Listing (paper copy and computer readable form)
Sequence Statement under 37 C.F.R. § § 1.821 (f) and (g)

VERSION OF CLAIMS WITH MARKINGS TO SHOW CHANGES MADE

The claims have been amended as follows:

1. (Amended) An isolated and/or recombinant nucleotide sequence enabling a G2/M cell cycle dependent initiation of translation of mRNA, wherein said isolated or recombinant nucleotide sequence is an internal ribosomal entry site sequence which initiates mRNA translation in a eukaryotic cell.
4. (Amended) An isolated and/or recombinant nucleic acid molecule encoding at least a functional part of an eukaryotic internal ribosomal entry site, which said eukaryotic internal ribosomal entry site, in a mitotic PITSLRE protein kinase gene, comprises SEQ ID NO: 1 or a functional part of SEQ ID NO: 1 and wherein said eukaryotic internal ribosomal entry site initiates mRNA translation in a eukaryotic cell.
11. (Twice Amended) A chimeric gene comprising:
 - (a) the isolated and/or recombinant nucleotide sequence of claim 31, and
 - (b) one or more control sequences operably linked to said isolated and/or recombinant nucleotide sequence.
12. (Twice Amended) A vector comprising the isolated and/or recombinant ~~nucleic acid molecule~~ nucleotide sequence of claim 31.
14. (Twice Amended) A eukaryotic host cell comprising the ~~nucleic acid molecule~~ nucleotide sequence of claim 31.

17. (Twice Amended) A method of inducing a cell cycle dependent initiation of translation in a eukaryotic cell, said method comprising introducing the isolated and/or recombinant nucleotide sequence of claim 31 into said eukaryotic cell.

Claims 2, 3, 8-10, 18, 19 and 22 have been cancelled without prejudice or disclaimer.

The following claims 25-36 have been added:

25. An isolated and/or recombinant nucleic acid molecule selected from the group consisting essentially of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, or combinations thereof, said nucleic acid molecule initiating the translation of mRNA in a eukaryotic cell.

26. A method of inducing a cell cycle dependent initiation of translation in a eukaryotic cell, said method comprising introducing the isolated and/or recombinant nucleic acid molecule of claim 25 into said eukaryotic cell.

27. A chimeric gene comprising:
a) the isolated and/or recombinant nucleic acid molecule of claim 25, and
b) one or more control sequences operably linked to said isolated and/or recombinant nucleic acid molecule.

28. A vector comprising the isolated and/or recombinant nucleic acid molecule of claim 25.

29. The vector of claim 28 wherein said vector is an expression vector, said vector further comprising a promoter.

30. A eukaryotic host cell comprising the nucleic acid molecule of claim 25.

31. An expression system comprising the eukaryotic host cell of claim 30.

32. A vector comprising the chimeric gene of claim 27.

33. The vector of claim 32, wherein said vector is an expression vector, said vector further comprising a promoter.

34. A eukaryotic host cell comprising the chimeric gene of claim 27.

35. An expression system comprising the eukaryotic host cell of claim 34.

36. An expression system comprising the eukaryotic host cell of claim 24.



APPENDIX C

**(VERSION OF CLAIMS AS AMENDED HEREIN
WITH MARKINGS TO SHOW CHANGES MADE)**

(Serial No. 09/915,060)